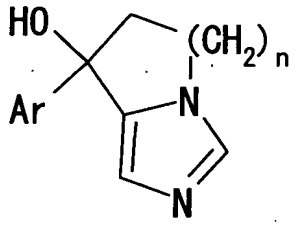
CLAIMS

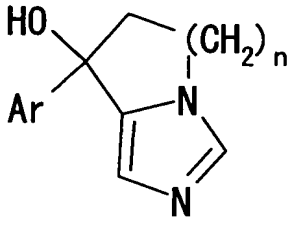
1. A controlled release composition for oral administration, which comprises a physiologically active substance which is a compound represented by the formula:



(I)-A

wherein n is an integer of 1 to 3, and Ar is an aromatic ring which may be substituted,
or a salt thereof, and a hydrophilic polymer.

2. A controlled release composition for oral administration, wherein a core containing a physiologically active substance which is a compound represented by the formula:



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wherein n is an integer of 1 to 3, and Ar is an aromatic ring which may be substituted,or a salt thereof is coated with a coating layer containing a polymer.

3. The controlled release composition according to claim 1 or 2, wherein the solubility (37°C) of the physiologically active substance with respect to 1st fluid for the disintegration test in the Japanese Pharmacopoeia is about 0.1 mg/mL or more.

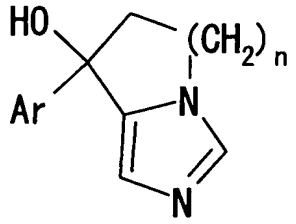
4. The controlled release composition according to claim 1, which has the following dissolution characteristics:

1) in Method 2 of the dissolution test in the Japanese Pharmacopoeia (paddle method, rotation speed of paddle: 50 rpm, 37°C) using 900 mL of 1st fluid for the disintegration test in the Japanese Pharmacopoeia, the dissolution rate of the physiologically active substance from the controlled release composition at 15 minutes after initiation of the test is less than 40%, and

2) in Method 2 of the dissolution test in the Japanese Pharmacopoeia (paddle method, rotation speed of paddle: 50 rpm, 37°C) using 900 mL of 2nd fluid for the disintegration test in the Japanese Pharmacopoeia, the dissolution rate of the physiologically active substance from the controlled release composition at 24 hours after initiation of the test is 40% or more.

5. A controlled release composition for oral administration, which comprises

(1) a physiologically active substance which is a compound represented by the formula:



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wherein n is an integer of 1 to 3, and Ar is an aromatic ring which may be substituted,
or a salt thereof,
(2) a hydrophilic polymer selected from hydroxypropylcellulose, hydroxypropylmethylcellulose, methylcellulose, polyethylene oxide, sodium carboxymethylcellulose and low-substituted hydroxypropylcellulose, and
(3) a lubricant selected from magnesium stearate, calcium stearate, talc, light anhydrous silicic acid, colloidal silica, synthetic aluminum silicate and magnesium aluminometasilicate.

6. The controlled release composition according to claim 2, which has the following dissolution characteristics:

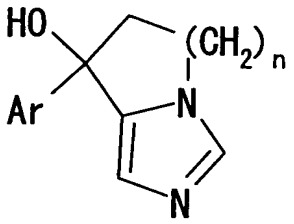
1) in Method 2 of the dissolution test in the Japanese Pharmacopoeia (paddle method, rotation speed of paddle: 50 rpm, 37°C) using 900 mL of 1st fluid for the disintegration test in the Japanese Pharmacopoeia, the dissolution rate of

the physiologically active substance from the controlled release composition at 15 minutes after initiation of the test is less than 10%, and

2) in Method 2 of the dissolution test in the Japanese Pharmacopoeia (paddle method, rotation speed of paddle: 50 rpm, 37°C) using 900 mL of 2nd fluid for the disintegration test in the Japanese Pharmacopoeia, the dissolution rate of the physiologically active substance from the controlled release composition at 24 hours after initiation of the test is 40% or more.

7. A controlled release composition for oral administration, wherein

(A) a core containing (1) a physiologically active substance which is a compound represented by the formula:



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wherein n is an integer of 1 to 3, and Ar is an aromatic ring which may be substituted, or a salt thereof, and (2) hydrophilic polymers selected from hydroxypropylcellulose, hydroxypropylmethylcellulose, methylcellulose, polyethylene oxide, sodium carboxymethylcellulose and low-substituted hydroxypropylcellulose, is coated with

(B) a coating layer containing (1) a enteric coating agent selected from cellulose acetate phthalate, hydroxypropylmethylcellulose phthalate, hydroxymethylcellulose acetate succinate and methacrylic acid copolymers, (2) a lubricant selected from magnesium stearate, calcium stearate, talc, light anhydrous silicic acid, colloidal silica, synthetic aluminum silicate and magnesium aluminometasilicate, and (3) a plasticizer selected from acetyl tributyl citrate, acetyl triethyl citrate, castor oil, diacetylated monoglyceride, dibutyl sebacate, diethyl phthalate, glycerin, mono- and diacetylated monoglyceride, polyethylene glycol, propylene glycol, triacetin and triethyl citrate.

8. The controlled release composition according to claim 2, wherein the release property of the physiologically active substance in the absence of the coating layer is of rapid release.

9. The controlled release composition according to claim 2, wherein the core is a controlled release matrix which further comprises a hydrophilic polymer.

10. The controlled release composition according to claim 1 or 9, wherein the content of the hydrophilic polymer is

about 3% to about 95% by weight.

11. The controlled release composition according to claim 2, wherein the polymer in the coating layer exhibits pH-dependent or delayed-dissolution type water solubility.

12. The controlled release composition according to claim 2, wherein the polymer in the coating layer is insoluble or sparingly soluble in water.

13. A controlled release composition, wherein the controlled release composition according to claim 1 or 2 is coated with a coating layer which contains a physiologically active substance which is identical with or different from the physiologically active substance contained in the above-mentioned controlled release composition, and the release property of the physiologically active substance being of rapid release.

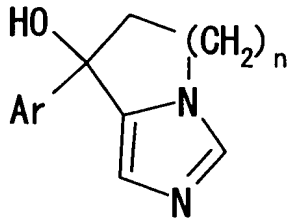
14. The controlled release composition according to claim 1 or 2, which is used for prevention or treatment of prostate cancer or breast cancer.

15. A composition which comprises the controlled release composition according to claim 1 or 2, combined with at

least one other controlled release composition wherein a release rate of a physiologically active substance is different from that of the above-mentioned controlled release composition.

16. The composition according to claim 15, wherein the other controlled release composition contains a physiologically active substance whose solubility (37°C) with respect to 1st fluid for the disintegration test in the Japanese Pharmacopoeia is about 0.1 mg/mL or more.

17. The composition according to claim 16, wherein the physiologically active substance in the other controlled release composition is a compound represented by the formula:



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wherein n is an integer of 1 to 3, and Ar is an aromatic ring which may be substituted,
or a salt thereof.

18. The composition according to claim 17, which has the following dissolution characteristics:

1) in Method 2 of the dissolution test in the Japanese Pharmacopoeia (paddle method, rotation speed of paddle: 50 rpm, 37°C) using 900 mL of 1st fluid for the disintegration test in the Japanese Pharmacopoeia, the dissolution rate of the physiologically active substance from the controlled release composition at 15 minutes after initiation of the test is less than 10%, and

2) in Method 2 of the dissolution test in the Japanese Pharmacopoeia (paddle method, rotation speed of paddle: 50 rpm, 37°C) using 900 mL of 2nd fluid for the disintegration test in the Japanese Pharmacopoeia, the dissolution rate of the physiologically active substance from the controlled release composition at 24 hours after initiation of the test is 20% or more.

19. The composition according to claim 15, wherein the release property of the physiologically active substance in the other controlled release composition is of rapid release.

20. The composition according to claim 15, wherein the other controlled release composition is prepared by coating a core containing a physiologically active substance with a coating layer containing a polymer which exhibits pH-dependent or delayed-dissolution type water solubility.

21. The composition according to claim 15, which is used for prevention or treatment of prostate cancer or breast cancer.

22. A controlled release composition for oral administration, which comprises
(1) (+)-6-(7-hydroxy-6,7-dihydro-5H-pyrrolo[1,2-c]imidazol-7-yl)-N-methyl-2-naphthamide or a salt thereof,
(2) a hydrophilic polymer selected from hydroxypropylcellulose, hydroxypropylmethylcellulose, methylcellulose, polyethylene oxide, sodium carboxymethylcellulose and low-substituted hydroxypropylcellulose,
(3) a disintegrant selected from lactose, sucrose, starch, carboxymethylcellulose, calcium carboxymethylcellulose, sodium croscarmellose, sodium carboxymethyl starch, light anhydrous silicic acid and low-substituted hydroxypropylcellulose,
(4) a lubricant selected from magnesium stearate, calcium stearate, talc, light anhydrous silicic acid, colloidal silica, synthetic aluminum silicate and magnesium aluminometasilicate,
(5) a enteric coating agent selected from cellulose acetate phthalate, hydroxypropylmethylcellulose phthalate, hydroxymethylcellulose acetate succinate and methacrylic

acid copolymers,

(6) a binder selected from α-starch, sugar, gelatin, gum arabic, methylcellulose, carboxymethylcellulose, sodium carboxymethylcellulose, crystalline cellulose, sucrose, D-mannitol, trehalose, dextrin, pullulan, hydroxypropylcellulose, hydroxypropylmethylcellulose and polyvinylpyrrolidone, and

(7) a plasticizer selected from acetyl tributyl citrate, acetyl triethyl citrate, castor oil, diacetylated monoglyceride, dibutyl sebacate, diethyl phthalate, glycerin, mono- and diacetylated monoglyceride, polyethylene glycol, propylene glycol, triacetin and triethyl citrate.

23. A controlled release composition for oral administration, wherein

(A) a core containing (1) (+)-6-(7-hydroxy-6,7-dihydro-5H-pyrrolo[1,2-c]imidazol-7-yl)-N-methyl-2-naphthamide or a salt thereof, and (2) a hydrophilic polymer selected from hydroxypropylcellulose, hydroxypropylmethylcellulose, methylcellulose, polyethylene oxide, sodium carboxymethylcellulose and low-substituted hydroxypropylcellulose, is coated with

(B) a coating layer containing (1) an enteric coating agent selected from cellulose acetate phthalate, hydroxypropylmethylcellulose phthalate,

hydroxymethylcellulose acetate succinate and methacrylic acid copolymers, (2) a lubricant selected from magnesium stearate, calcium stearate, talc, light anhydrous silicic acid, colloidal silica, synthetic aluminum silicate and magnesium aluminometasilicate, and (3) a plasticizer selected from acetyl tributyl citrate, acetyl triethyl citrate, castor oil, diacetylated monoglyceride, dibutyl sebacate, diethyl phthalate, glycerin, mono- and diacetylated monoglyceride, polyethylene glycol, propylene glycol, triacetin and triethyl citrate.